## II. RESPONSE TO OFFICE ACTION

*A. Status of the Claims*

Claims 1-39 were pending prior to the Office Action dated October 6, 2005. Claims 1, 8, 24 and 39 have been cancelled without prejudice, and claims 2, 11, 13, 14, 15, 17, 19, 20, 22, 23, and 25 have been amended. No new matter has been added. Claims 2-7, 9-23 and 25-38 are pending and under examination.

*B. Specification*

The specification has been amended to capitalize the trademarks IMMORTOMOUSE® and XENOMOUSE®. It is believed that the appropriate generic terminology is already provided in the specification the first time these terms are used. See, *e.g.*, page 9, line 13 and top of page 16.

*C. Claim Rejections – 35 U.S.C. §112, 2nd Paragraph*

With respect to the rejection of claim 8, which references "hybridoma culture medium," it is submitted that such medium is well known to those of skill in the art and such medium is indeed commercially available. Nonetheless, Applicants agree that there might be slight, albeit inconsequential, differences between different commercially available hybridoma culture mediums and thus have elected to simply cancel the claim to obviate the rejection.

With respect to the Examiner's concerns regarding claim 25, it is noted that the claim contained various typographical errors and these have now been corrected.

*D. Claim Rejections – 35 U.S.C. §112, 1st Paragraph*

Applicants note the Examiner's concerns with respect to the therapeutic aspects of claims 24 and 39. While it is submitted that the use of monoclonal antibodies in therapy was, at the time of filing, was routine and that numerous such antibodies were FDA-approved, Applicants

have elected to progress the case to allowance by canceling these claims without prejudice for re-presentation in potential continuing applications at a future date.

*E. Claim Rejections – 35 U.S.C. §102*

It is noted that claim 2 has been placed into independent form and claim 1 has been cancelled. Thus, the claims are now free of all anticipation rejections.

*F. Claim Rejections – 35 U.S.C. §103*

It is first noted that the rejections set forth in paragraphs 20 though 23 of the Action have been obviated through the cancellation of claim 1 and amendment of claim 2 into independent form. Thus, the only rejections remaining are those set forth in paragraphs 24-28 of the Action, which Applicants will now address.

The remaining rejections are based on the Action's contention that Harlow in view of Jat (as evidenced by Kano and Kaki) renders obvious the preparation of monoclonal antibody-producing cells without forming hybridomas. We strongly disagree. The text in Harlow apparently relied upon by the Action is found at page 148, in the section entitled "Production of Monoclonal Antibodies," which reads as follows:

> Figure 6.3 outlines the steps in the production of monoclonal antibodies. Animals are injected with an antigen preparation, and once a good humoral response as appeared in the immunized animal, and appropriate screening procedure is developed. There sera from test bleeds are used to develop and validate the screening procedure. After an appropriate screen has been established, the actual production of the hybridomas can begin. Several days prior to the fusion, animals are boosted with a sample of the antigen. For the fusion, antibody-secreting cells are prepared from the immunized animal, mixed with the myeloma cells, and fused/. After the fusion, cells are diluted in selective medium and plated in multiwell tissue culture dishes. Hybridomas are ready to test beginning about 1 week after the fusion. Cells from positive wells are grown and then single-cell cloned. Hybridomas production seldom takes less than 2 months from start to finish, and it can take well over a year. It is convenient to divide the production of monoclonal antibodies into three stages: (1) immunizing mice, (2) developing the screening procedure, and (3) producing hybridomas. Any one of these stages may proceed very quickly, but all have inherent problems that should be

considered prior to the start of the project, and these areas are discussed separately below.

However, it is clear from this excerpt that Harlow *specifically teaches* that hybridoma formation is *an absolute requirement* for the production of monoclonal antibodies. In this regard, it must be remembered that "[a] person of ordinary skill in the art is ... presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights." *Standard Oil Co. v. American Cyanamid Co.*, 227 USPQ 293, 298 (Fed. Cir. 1985). Thus, one of ordinary skill in the monoclonal antibody art would most certainly follow the "conventional wisdom" of Harlow by using hybridomas to form monoclonal antibodies. Thus, there would be neither need nor motivation for the ordinarily skilled worker to employ an alternative approach and instead use the conditionally immortal cells of the transgenic Jat mouse.

Indeed, upon viewing Harlow, there is simply no evidence of a problem to be solved! Courts have long held that to render a claimed invention obvious, the prior art must recognize the source or existence of the problem in the first place. For example, the U.S. Supreme Court has held that in the case of a known problem, the identification of the source of that problem is patentable, even where the solution is obvious once the source is known. *Eibel Process Co. v. Minnesota & Ontario Paper Co.*, 261 U.S. 45, 68 (1923). Similarly, a "patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified." *In re Sponnoble*, 160 U.S.P.Q. 237, 243 (C.C.P.A. 1969). A corollary to these principles is where the prior art fails to recognize the existence of a problem in the first place. In this regard, the CCPA has held that it is improper to conclude that an invention is obvious absent evidence that one of skill would have recognized that an underlying problem existed. *In re Nomiya*, 184 U.S.P.Q. 607 (CCPA 1975).

The Action's only attempt to argue the existence of a motivation for one of ordinary skill to employ cells of the Jat mouse to produce hybridomas is in paragraph 27 of the Action, which states merely that such a procedure is "simple." While we do not disagree that that procedure is relatively straightforward to carry out, we note that §103(a) specifically states that "patentability shall not be negatived by the manner in which the invention was made." In other words, the fact that the development of an invention might have been relatively straightforward is totally irrelevant to the obviousness inquiry. See, *e.g.*, *In re Kratz*, 592 F.2d 1169, 201 U.S.P.Q. 71 (CCPA 1979), citing the foregoing passage of §103 in holding that the relative ease of making a discovery can not be considered in deciding obviousness.

With respect to the claims directed to the production of human monoclonals, the Action introduces the teachings of Green, which relates to the Xenomouse. However, Green fails to in any way teach or suggest the use of the Xenomouse to immortalize antibody-producing cells by inducing a transforming oncogene, and thus in no way completes the foregoing obviousness rejection. The Examiner apparently concedes this point in that Green is cited merely for the proposition that the Xenomouse could be used to produce human antibodies "due to the advantages related to clinical applications." Even then, though, the Action fails to identify any specific teaching within either Jat or Green that would motivate the ordinarily skilled worker to cross the Green mouse with the Jat mouse.

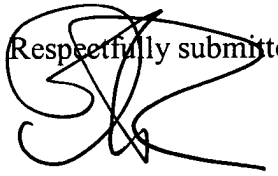
Thus, for the foregoing reasons it is submitted that the Examiner has failed to set forth a *prima facie* case of obviousness and Applicants thus respectfully request that the rejection be withdrawn.

## CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3055 is respectfully requested.

Respectfully submitted,



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